PATENT COOPERATION TREATY

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INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY
(Chapter I of the Patent Cooperation Treaty)

(PCT Rule 44*bis*)

Applicant's or agent's file reference 101368-1 WO	**FOR FURTHER ACTION**	See item 4 below
International application No. PCT/SE2005/000221	International filing date *(day/month/year)* 17 February 2005 (17.02.2005)	Priority date *(day/month/year)* 20 February 2004 (20.02.2004)
International Patent Classification (8th edition unless older edition indicated) See relevant information in Form PCT/ISA/237		
Applicant ASTRAZENECA AB		

1. This international preliminary report on patentability (Chapter I) is issued by the International Bureau on behalf of the International Searching Authority under Rule 44 *bis*.1(a).

2. This REPORT consists of a total of 6 sheets, including this cover sheet.

   In the attached sheets, any reference to the written opinion of the International Searching Authority should be read as a reference to the international preliminary report on patentability (Chapter I) instead.

3. This report contains indications relating to the following items:

☒	Box No. I	Basis of the report
☐	Box No. II	Priority
☐	Box No. III	Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
☐	Box No. IV	Lack of unity of invention
☒	Box No. V	Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
☐	Box No. VI	Certain documents cited
☐	Box No. VII	Certain defects in the international application
☐	Box No. VIII	Certain observations on the international application

4. The International Bureau will communicate this report to designated Offices in accordance with Rules 44*bis*.3(c) and 93*bis*.1 but not, except where the applicant makes an express request under Article 23(2), before the expiration of 30 months from the priority date (Rule 44*bis* .2).

	Date of issuance of this report 22 August 2006 (22.08.2006)
The International Bureau of WIPO 34, chemin des Colombettes 1211 Geneva 20, Switzerland Facsimile No. +41 22 338 82 70	Authorized officer Philippe Becamel e-mail: pt12@wipo.int

Form PCT/IB/373 (January 2004)

PATENT COOPERATION TREATY

From the
INTERNATIONAL SEARCHING AUTHORITY

To:
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PCT

WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY

(PCT Rule 43*bis*.1)

Date of mailing *(day/month/year)*	19-05-2005
Applicant's or agent's file reference 101368-1 WO	**FOR FURTHER ACTION** See paragraph 2 below

International application No.	International filing date *(day/month/year)*	Priority date *(day/month/year)*
PCT/SE 2005/000221	17.02.2005	20.02.2004

International Patent Classification (IPC) or both national classification and IPC
C07D 401/12, A61K 31/4439, A61P 1/04

Applicant
AstraZeneca AB et al

1. This opinion contains indications relating to the following items:
   - ☒ Box No. I Basis of the opinion
   - ☐ Box No. II Priority
   - ☐ Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
   - ☐ Box No. IV Lack of unity of invention
   - ☒ Box No. V Reasoned statement under Rule 43*bis*.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
   - ☐ Box No. VI Certain documents cited
   - ☐ Box No. VII Certain defects in the international application
   - ☐ Box No. VIII Certain observations on the international application

2. **FURTHER ACTION**

   If a demand for international preliminary examination is made, this opinion will be considered to be a written opinion of the International Preliminary Examining Authority ("IPEA") except that this does not apply where the applicant chooses an Authority other than this one to be IPEA and the chosen IPEA has notified the International Bureau under Rule 66.1*bis*(b) that written opinions of this International Searching Authority will not be so considered.

   If this opinion is, as provided above, considered to be a written opinion of the IPEA, the applicant is invited to submit to the IPEA a written reply together, where appropriate, with amendments, before the expiration of 3 months from the date of mailing of Form PCT/ISA/220 or before the expiration of 22 months from the priority date, whichever expires later.

   For further opinions, see Form PCT/ISA/220.

3. For further details, see notes to Form PCT/ISA/220.

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WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY

International application No.
PCT/SE 2005/000221

Box No. I Basis of this opinion

1. With regard to the **language**, this opinion has been established on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.

   ☐ This opinion has been established on the basis of a translation from the original language into the following language, _____, which is the language of a translation furnished for the purposes of international search (under Rules 12.3 and 23.1(b)).

2. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application and necessary to the claimed invention, this opinion has been established on the basis of:

   a. type of material

   ☐ a sequence listing

   ☐ table(s) related to the sequence listing

   b. format of material

   ☐ in written format

   ☐ in computer readable form

   c. time of filing/furnishing

   ☐ contained in the international application as filed.

   ☐ filed together with the international application in computer readable form.

   ☐ furnished subsequently to this Authority for the purposes of search.

3. ☐ In addition, in the case that more than one version or copy of a sequence listing and/or table relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.

4. Additional comments:

WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY

International application No.
PCT/SE 2005/000221

Box No. V **Reasoned statement under Rule 43*bis*.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement**

1. Statement

Novelty (N)	Claims	1-7	YES
	Claims	8-9	NO
Inventive step (IS)	Claims		YES
	Claims	1-9	NO
Industrial applicability (IA)	Claims	1-9	YES
	Claims		NO

2. Citations and explanations:

The following documents are cited in the search report:

D1 WO 9602535 A1
D2 WO 03097606 A1
D3 WO 0104109 A1
D4 WO 9840378 A1
D5 WO 9828294 A1
D6 WO 03089408 A2

The claimed invention relates to enantiomer or enantiomerically enriched form of 5-methoxy-2[[4-sub.-3,5-dimethyl-2-pyridinyl)methyl]sulfinyl]1-H-bensimidazole derivatives and 5-methoxy-2[[4-sub.-3,5-dimethyl-1-oxido-2-pyridinyl) methyl]sulfinyl]1-H-bensimidazol derivatives and tautomers thereof as intermediates in the synthesis of the S- or R-enantiomer of 5-methoxy-2[[4-methoxy-3,5-dimethyl-2-pyridinyl)methyl]sulfinyl]1-H-bensimidazole.

D1, which is regarded as being the closest prior art, discloses an enantioselective synthesis of single enantiomers of omeprazole. The claimed process is an asymmetric oxidation of a pro-chiral sulphide to a single enantiomer or an enantiomerically enriched form of a corresponding sulphoxide. The application also relates to their use in medicine. The process is characterized by an asymmetric oxidation in an organic solvent of a pro-chiral sulphide with an oxidising agent and a chiral titanium complex, optionally in the presence of a base (see page 14). The claimed process in claim 6 and the known process will be

.../...

Supplemental Box

In case the space in any of the preceding boxes is not sufficient.
Continuation of: Box V

carried out with the same oxidising agent and under the same reaction conditions.

The claimed process differs from the known in that the starting compounds do not contain the same substitution in the 4-position.

The problem to be solved will be regarded as to first oxidise a pro-chiral sulphide with a substitution in the 4-position which differs from a methoxy-group to the corresponding sulphinyl-group and then replace the substitution in the 4-position to a methoxy-group.

A solution to that problem is found in D2, which discloses on pages 9 and 10 a replacement of a substitute in the 4-position by a methoxile group to the corresponding methoxi-group.

The same solution is to be found in D3 example 7 where a 4-nitro-group is replaced by a 4-methoxi-group with a solution of sodium methoxide in methanol. This replacement can be done after an oxidation of a sulphide group to a sulphinyl group (see example 6).

Considering what is known from D1 and D2 or D3, it is considered to lie within the skills of a person skilled in the art to prepare the claimed intermediates with a similar known process and to use them in a process to prepare the S- or R-entiomer of 5-methoxy-2[[4-methoxy-3,5-dimethyl-2-pyridinyl)methyl]sulfinyl]1-H-bensimidazole. If it can be shown that some aspect covered by claims 1-7 provides unexpected effects and the claims are restricted accordingly, the judgement may be reconsidered. Until these conditions are met, claims 1-7 are not considered to involve an inventive step. As no other effect than the claimed has been shown, the invention as defined in claims 1-7 lacks inventive step.

.../...

WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY

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Supplemental Box

In case the space in any of the preceding boxes is not sufficient.
Continuation of: Box V

D1 discloses a single enantiomer or an enatiomeriacally enriched form of e.g. omeprazole see claims 24 and 25 thus claims 8 and 9 lack novelty.

Claims for a product defined in terms of a process of manufacture are admissible only if the product as such fulfils the requirements for patentability, i.e. inter alia that it is new and inventive. A product is not rendered novel merely by the fact that it is produced by means of a new process. Therefore, the subject-matter of claims 8 and 9 is not new with regard to D1.

D4, D5 and D6 disclose the general state of the art, and are not considered to be of particular relevance.